

# Whole body [ $^{18}\text{F}$ ]fluorodeoxyglucose positron emission tomography imaging for the diagnosis of pacemaker or implantable cardioverter defibrillator infection: a preliminary prospective study

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## Abstract

We studied the potential use of [ $^{18}\text{F}$ ]fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) whole body positron emission tomography (PET)-computed tomography for the diagnosis of device infection and extension of infection. Twenty-one patients with suspected device infection were prospectively included and compared with 14 controls free of infection.  $^{18}\text{F}$ -FDG uptake on the box and on the leads was visually and quantitatively interpreted (using the maximal standard uptake value). The final diagnosis was obtained either from bacteriological data after device culture ( $n = 11$ ) or by a 6-month follow-up according to modified Duke's criteria ( $n = 10$ ). Ten patients finally showed infection on bacteriological study ( $n = 8$ ) or during follow-up ( $n = 2$ ). Sensitivity, specificity, positive predictive value and negative predictive value were, respectively, 80%, 100%, 100% and 84.6% on patient-based analysis (presence or absence of infection). They were 100%, 100%, 100% and 100% for boxes, but only 60%, 100%, 100% and 73% for leads. Quantitative analysis could be useful for boxes but not for leads, for which the presence of a mild hot spot was the best criterion of infection. The four false negatives on leads received antibiotics for longer than the six true positives ( $20 \pm 7.2$  vs.  $3.2 \pm 2.3$  days,  $p < 0.01$ ). Although the study was not designed for this purpose, management could have been modified by PET results in six of 21 patients.  $^{18}\text{F}$ -FDG PET imaging may be useful for the diagnosis of device infection, and could impact on clinical management. Interpretation of negative cases should be performed with caution if patients have received antibiotics.

**Keywords:**  $^{18}\text{F}$ -FDG, infection, pacemaker, PET-CT

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## Introduction

After pacemaker (PM) or implantable cardioverter-defibrillator (ICD) implantation, device infection of box and/or leads, although rare (0.5–5%, according to the most recent series, giving an average of 2%) [1,2], is a feared and serious complication, leading to combined double antibiotherapy with complete extraction of the material before discussion of secondary re-implantation.

A positive diagnosis of box infection (or, more precisely, infection of the pocket in which the box is implanted) may

be clinically suspected in cases of external suppuration, but usually requires bacteriological samples to demonstrate septicaemia, associated with transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) to confirm images suggestive of vegetation on leads.

However, even when vegetation is demonstrated, differential diagnosis between infection and thrombus may be difficult [3]. Furthermore, infection staging and identification of other septic locations may be very important in order to monitor treatment efficacy before any re-implantation.

Inflammatory cells have a high affinity for [ $^{18}\text{F}$ ]fluorodeoxyglucose ( $^{18}\text{F}$ -FDG), which explains the use of  $^{18}\text{F}$ -FDG positron emission tomography (PET) imaging in pathological processes that involve lymphocytes, plasmocytes and or/ macrophage infiltration [4–9]. Although neutrophils are the hallmark of prosthetic infection,  $^{18}\text{F}$ -FDG uptake of mononuclear cells has been used for the diagnosis of infection such

as prosthetic infection [4–6], tuberculosis [7] or vascular prosthesis [9]. Therefore, whole body <sup>18</sup>F-FDG PET imaging could be useful for the diagnosis of device infection. Nevertheless, <sup>18</sup>F-FDG PET imaging is not free of potential pitfalls. First, the mechanical rubbing of the box against muscles and/or soft tissue may lead to mild inflammation, and falsely increase both <sup>18</sup>F-FDG uptake and as electrical stimulation of surrounding muscles owing to electrical leakage from the box. Second, in the case of infection, the size of the leads (1.5–3 mm in diameter) and of the vegetation might be below the PET–computed tomography (CT) spatial resolution (7 mm), impairing interobserver reproducibility and diagnostic accuracy if <sup>18</sup>F-FDG uptake is not very high.

The present study aimed: (i) to prospectively evaluate the use of <sup>18</sup>F-FDG PET-CT whole body imaging in patients suspected of having sepsis after PM or ICD implantation for positive diagnosis of infection and identification of other septic locations; (ii) to define the best methodology for image analysis (i.e. visual or quantitative interpretation); and (iii) to assess interobserver reproducibility.

To quantify <sup>18</sup>F-FDG uptake and determine abnormal threshold values, a control population was prospectively selected, consisting of asymptomatic patients referred to our institution for oncological indications and undergoing PM or ICD implantation at least 1 year before PET study, with stable disease and without any clinical or biological symptoms of infection.

## Materials and Methods

### Population: group 1

All patients suspected of having device infection were consecutively included from 8 August 2007 to 15 September 2009. Device sepsis was clinically suspected because of: (i) unexplained persistent or recurrent fever >38°C, and/or (ii) chronic inflammatory syndrome with increased C-reactive protein, and/or (iii) positive blood culture independently of the TTE and TEE results, and/or (iv) clinical suspicion of pocket infection on the basis of inflammation and/or liquid effusion. Consent was obtained from all patients before examination, although <sup>18</sup>F-FDG-PET has approval in France for location of occult infection or in cases of fever of unknown origin. These patients constituted group 1. Analysis was independent of sex, age, reason for implantation, date of implantation and device type.

### Control group: group 2

In the same time period, 14 patients with asymptomatic implanted PM, referred for PET-CT imaging in our institution

for oncological purposes, were prospectively included. Patients were selected independently of sex, age and reason for implantation. Clinical and biological infectious syndrome was an exclusion criterion, but did not, in fact, occur in this group.

### Final diagnosis

The decision on device extraction was made without taking account of PET results. However, in the case of other septic locations being discovered on PET, this information was transmitted to the clinician. The final diagnosis of presence or absence of infection was based either on bacteriology (blood culture or device analysis performed after device extraction) or, when no device was extracted, on a prolonged follow-up of 6 months with modified Duke's criteria [10]. Patients with clinical suspicion of device infection and presenting infectious endocarditis according to these criteria were considered to be positive for device infection. Diagnosis was ruled out if clinical symptoms and/or biological abnormalities returned to normal during this follow-up without fulfilling the modified Duke's criteria; if not, and if no other aetiology was found, device extraction was decided on.

### <sup>18</sup>F-FDG PET acquisition

Whole body PET-CT imaging was performed on a dedicated Philips Gemini PET/CT system (Philips Medical Systems, Andover, MA, USA) after intravenous administration of 5 MBq/kg of <sup>18</sup>F-FDG (maximum, 500 MBq) in patients at rest, after an 8-h fasting period. PET-CT imaging was performed 1 h after <sup>18</sup>F-FDG injection, with scanning from the base of the skull to above knee level. The CT acquisition parameters were as follows: 4-mm-thick transaxial images; pitch, 1.5; 120 kV and 120–160 mAs; slice thickness, 5 mm with rebuilding in 2-mm slices every 2 mm; pitch, 1; collimation, 16 × 1.5; standard resolution; and field of view, 600 mm. No oral or intravenous contrast was used. PET data were acquired in three-dimensional mode, at 2 min per step. Non-attenuation-corrected slices, slices corrected for attenuation by an iterative method (three-dimensional high-resolution Row Action Maximum Likelihood Algorithm) and a CT attenuation map were reconstructed. The native PET slice thickness was 4 mm. Glycaemia was controlled at the time of the study, and was <9 mM in all consecutive patients, even though glycaemia was not a criterion for patient exclusion.

### Data management

*Visual analysis.* Data for both groups were first visually analysed by two independent observers, blind to the clinical and

bacteriological data and to the other imaging modalities, on a Brilliance 190 XP monitor (Philips Healthcare, Cleveland, OH, USA). Image interpretation initially consisted of quality control with maximum intensity projection analysis; visual analysis was then performed with attenuation-corrected and non-attenuation-corrected images and fusion with CT slices for each dataset. Then, on the basis of the presence and intensity of hot spots around box and/or leads in group 1 patients, each observer classified the case as positive or negative for box infection, lead infection and device infection, independently of the septic location.

**Quantitative analysis.** In group 1, quantitative analysis was carried out by computing  $^{18}\text{F}$ -FDG maximal standard uptake value ( $\text{SUV}_{\text{max}}$ ) inside a circular region of interest (ROI) of 5-mm radius around the most intense uptake over the cutaneous side of the box, over the muscle side of the box and over each hot spot on the leads, when present, or else over the most intense  $^{18}\text{F}$ -FDG uptake spot over the leads, with a maximum of five ROIs on the leads.

Similar ROIs were drawn in group 2 over the boxes. As none of the patients in this control group showed visually significant uptake over the leads, ROIs were placed over the leads on standardized slices defined as crossing the middle of the body of the second, fifth and seventh vertebrae.

### Statistical analysis

Interobserver reproducibility was evaluated with a Cohen kappa test [11] for qualitative data (presence or absence of infection on box, lead or both), and judged to be bad for kappa <0.20, poor between 0.21 and 0.40, average between 0.41 and 0.6, fair between 0.61 and 0.8, and excellent above 0.81. A final consensus reading was performed in the case of discrepancies.

Quantitative data were compared with paired or non-paired *t*-tests, as appropriate; a *p*-value <0.05 was considered to be significant.

## Results

### Population

**Patients suspected of device infection: group 1 (*n* = 21).** Twenty-one patients were prospectively included. Devices were PMs in 18 patients and ICDs in three, all implanted in the thorax. Device infection was suspected because of: (i) unexplained persistent or recurrent fever >38°C (*n* = 17), and/or (ii) chronic inflammatory syndrome with increased C-reactive protein (*n* = 15), and/or (iii) positive blood

culture (*n* = 11) independently of the TTE and TEE results, and/or (iv) clinical suspicion of pocket infection on the basis of inflammation and/or liquid effusion (*n* = 5) (Table 1).

Fifteen of the 21 patients were receiving antibiotic treatment at the time of PET-CT imaging, for a mean  $12.05 \pm 7$  days.

Devices were explanted from 11 patients (one later, during follow-up) and bacteriological proof of infection was obtained (by culture) for eight of them.

In the ten remaining (non-explanted) patients and during follow-up ( $8.3 \pm 2.6$  months), infection was confirmed in one patient on device culture (obtained post-mortem). Another showed three minor criteria for septicaemia [10]: persistent fever >38°C, positive blood culture (*Streptococcus mitis*) and mitral bioprosthesis for mitral regurgitation. This patient was considered to be positive and treated accordingly.

Thus, diagnosis of infection was confirmed in ten of 21 patients and was not confirmed in 11. The bacteria identified were: *Klebsiella pneumoniae* (*n* = 1), *Corynebacterium jeikeium* (*n* = 1), *Streptococcus sanguinis* (*n* = 1), *S. mitis* (*n* = 1), methicillin-resistant coagulase-negative *Staphylococcus* (*n* = 1), *Escherichia coli* (*n* = 1), *Pseudomonas aeruginosa* (*n* = 1), and methicillin-sensitive coagulase-negative *Staphylococcus* (*n* = 3).

In the 11 patients without confirmed device infection, symptoms disappeared during follow-up within  $2.3 \pm 0.9$  months in nine cases and persisted without further evidence of device sepsis in two others with a follow-up of  $7.3 \pm 1.2$  months. One of these two patients had a pattern of aortitis on PET images; the other had (previously known) sepsis of the tarsal bone.

### Echocardiographic findings

TTE was performed in all patients and TEE in 16. TTE was not performed in five patients, because of their clinical status.

TTE clearly demonstrated vegetations in two patients (confirmed by TEE).

TTE was questionable, showing a suspicious image of vegetation in three others. Nevertheless, infection was confirmed neither by the follow-up nor by TEE in two of them. TEE was not performed for the latter, because of his clinical status, but the follow-up showed an absence of device infection. TEE revealed vegetations in three other patients that were not seen with TTE.

**Control group: group 2 (*n* = 14).** The mean follow-up for the 14 control patients was  $18 \pm 6.4$  months, and all patients were free of any clinical or biological infectious event.

TABLE 1. Group I population

Group I	Department of origin	Clinical symptoms	Biological data	TEP	BC	Bacteria in BC	Echocardiographic results		Bacteria after explantation	FU	Final diagnosis
							TTE	TEE			
1	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	L	+	<i>Escherichia coli</i>	Negative	Negative	<i>E. coli</i>		+
2	Cardiology	Unexplained persistent or recurrent fever >38°C		–	+	<i>Staphylococcus</i>	Negative	Negative		8	–
3	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	–		Negative	Negative		7	–
4	Cardiology	Peak of fever >38°C for 48 h	Increased CRP	–	–		Questionable	Negative		11	–
5	Internal Medicine	Unexplained persistent or recurrent fever >38°C		–	+	<i>Staphylococcus</i>	Negative		Negative		–
6	Internal Medicine	Unexplained persistent or recurrent fever >38°C	Increased CRP	B	–		Negative	Negative	<i>Pseudomonas</i>		+
7	Cardiology	Clinical suspicion of pocket infection	Increased CRP	–	+	<i>Staphylococcus</i>	Negative			7	–
8	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	–		Negative	Positive	<i>Staphylococcus</i>		+
9	Cardiology	Unexplained persistent or recurrent fever >38°C, clinical suspicion of pocket infection	Increased CRP	P	–		Positive	Positive	<i>Streptococcus</i>		+
10	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	L	+	<i>Staphylococcus</i>	Negative	Negative	<i>Staphylococcus</i> post-mortem	6	+
11	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	–		Negative	Negative		8	–
12	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	L	+	<i>Staphylococcus</i>	Positive	Positive	<i>Staphylococcus</i>		+
13	Cardiology	Unexplained persistent or recurrent fever >38°C, clinical suspicion of pocket infection		B	+	<i>Klebsiella pneumonia</i>	Negative	Positive	<i>K. pneumonia</i>		+
14	Cardiology	Persistent biological syndrom >2 months	Increased CRP	–	+	<i>Staphylococcus</i>	Negative	Negative		9	–
15	Cardiology	Unexplained persistent or recurrent fever >38°C		–	+	<i>Staphylococcus</i>	Questionable		Negative		–
16	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	+	<i>Streptococcus mitis</i>	Negative			6	+
17	Cardiology	Unexplained persistent or recurrent fever >38°C, clinical suspicion of pocket infection		P	–		Negative		<i>Staphylococcus</i>		+
18	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	–		Negative	Negative		14	–
19	Cardiology	Clinical suspicion of pocket infection		–	–		Questionable	Negative	Negative	8	–
20	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	B	+	<i>Corynebacterium</i>	Negative	Positive	<i>Corynebacterium</i>		+
21	Cardiology	Unexplained persistent or recurrent fever >38°C	Increased CRP	–	–		Negative	Negative		7	–

B, both (pocket+lead infection); BC, blood culture; CRP, C-reactive protein; FU, follow-up (months); L, lead infection; P, pocket infection; ; TEE, transoesophageal; PET, positron emission tomography; TTE, transthoracic.

### Positive diagnosis of infection: visual analysis

In the 21 group I patients, visual analysis of PET images revealed 42 hot spots: 21 on the boxes and 21 on the leads.

On patient-based analysis, eight were true-positive, 11 true-negative, two false-negative and none false-positive, giving sensitivity, specificity, positive predictive value, negative predictive value and accuracy of, respectively, 80%, 100%, 100%, 84.6% and 90.4%. The explanted patient in whom device infection was not confirmed during follow-up had a negative PET finding, whereas the patient explanted 3 months later and for whom infection was bacteriologically proven (post-mortem) had a positive PET finding at the time of inclusion. The patient who had three minor criteria according to Duke's classification had a negative PET finding.

On site-by-site analysis, 27 devices were free of hot spots and were true-negative, and four were false-negative. Diagnostic accuracy was better for boxes (100%) than for leads (80.9%). For boxes, five hot spots were true-positive, all proven bacteriologically after device explantation (*C. jeikeium* (*n* = 1), *P. aeruginosa* (*n* = 1), *K. pneumonia* (*n* = 1), *S. sanguinis* (*n* = 1) and *Staphylococcus* (*n* = 1)), 16 boxes were true-negative, and none were false-negative or false-positive. Only three of the five patients with bacteriologically confirmed pocket infection were clinically suspected. In two patients referred for PET because of clinical suspicion of pocket infection, infection was not confirmed during a follow-up of more than 6 months, and symptoms disappeared 1 and 3 months after examination. For leads, six hot spots were true-positive,

11 patients did not show hot spots on leads and were true-negative, four were false-negative and none were false-positive (Table 2). Thus, sensitivity, specificity, positive predictive value and negative predictive value were all 100% for boxes and, respectively, 60%, 100%, 100% and 73% for leads.

Regarding lead infection, the four false-negative cases received antibiotic treatment for significantly longer than the six true-positive cases ( $20 \pm 7.2$  vs.  $3.2 \pm 2.3$  days;  $p < 0.01$ ).

### Extension of infectious disease

In four group 1 patients with bacteriologically proven infection,  $^{18}\text{F}$ -FDG PET revealed other unknown abnormalities: associated lung infection ( $n = 2$ , confirmed by CT and by follow-up), infection of right ventricle/pulmonary artery prosthetic tube ( $n = 1$ , confirmed by culture after surgery) and aortitis ( $n = 1$ , confirmed by TEE and follow-up). Furthermore, PET confirmed a sepsis of the tarsal bone in one other patient, which was clinically suspected, previously documented by bone scintigraphy and confirmed by biopsy.

### Interobserver reproducibility of visual analysis

Kappa values for patient classification (presence or absence of device infection), pocket infection (presence or absence) and lead infection (presence or absence) were, respectively, 0.80, 0.89 and 0.79.

### Quantitative analysis

**Boxes.** In controls (group 2), the mild, diffuse  $^{18}\text{F}$ -FDG uptake in soft tissue on the side of the box facing the muscles was significantly higher than that on the opposite side (skin):  $\text{SUV}_{\text{max}} = 1.70 \pm 0.52$  vs.  $1.13 \pm 0.48$ ;  $p < 0.01$ .

In group 1 patients with no box infection, the  $\text{SUV}_{\text{max}}$  values for  $^{18}\text{F}$ -FDG uptake on the muscle and skin sides were, respectively,  $1.95 \pm 0.61$  and  $1.22 \pm 0.57$  ( $p < 0.01$ ); these values were not significantly different from those of controls (group 2).

**TABLE 2.** Diagnostic accuracy according to site of infection: box only, leads only, box and leads (both sites) and box or leads (and then analysis on a patient basis)

	Box	Lead	Box and lead	Box and/or lead (patients)
True-positive	5	6	11	8
True-negative	16	11	27	11
False-positive	0	0	0	0
False-negative	0	4	4	2
Sensitivity (%)	100	60	73.3	80
Specificity (%)	100	100	100	100
PPV (%)	100	100	100	100
NPV (%)	100	73.3	87	84.6

PPV, positive predictive value; NPV, negative predictive value.

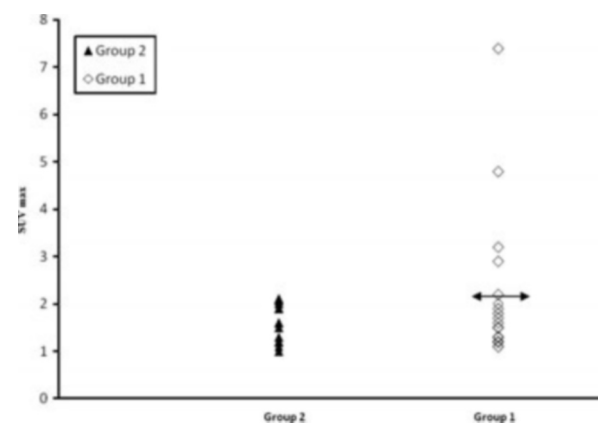
In patients with confirmed box infection, the involved sides showed greater and heterogeneous uptake, comprising diffuse uptake with more intense hot spots. Average uptake values were significantly higher than in controls (respectively,  $\text{SUV}_{\text{max}} = 4.72 \pm 1.68$  and  $1.70 \pm 0.52$ ;  $p < 0.01$ ).

An  $\text{SUV}_{\text{max}}$  cut-off value equal to or  $> 2.2$  (mean control value + 1 standard deviation) discriminated all infected patients from controls (Fig. 1).

**Leads.** Average  $^{18}\text{F}$ -FDG uptake was not significantly different between the two groups:  $\text{SUV}_{\text{max}} = 1.87 \pm 0.41$  (group 2) vs.  $1.68 \pm 0.38$  (group 1) (not significant (NS)). A slightly elevated focal uptake over the lead was more valuable for the diagnosis of sepsis than the overall uptake value itself.

## Discussion

Fifty thousand PMs per year and 43 ICDs per year and per million inhabitants are implanted in France. Infection of these devices may involve either the site of the box (pocket) (0.5–5% of cases) or the leads themselves (0.8–4.9% of cases) [1,2]. Thus, the incidence of device infection appears to be similar to that of other infections on prosthetic material. There is no established reference standard for assessing device infection. When, however, it is present, patients with device infection are managed as for endocarditis. We therefore used Modified Duke's criteria, the reference standard in



**FIG. 1.** Plot of standard uptake value of  $^{18}\text{F}$ fluorodeoxyglucose uptake around boxes between controls (group 2, left) and patients (group 1, right). A maximal standard uptake value ( $\text{SUV}_{\text{max}}$ ) threshold value equal to or  $> 2.2$  completely separates controls (left) and non-infected patients on the one hand (right column below the marker) and infected patients on the other hand.



endocarditis, comprising two major criteria: (i) typical organism in two separate blood cultures or persistently positive blood cultures; and (ii) presence of vegetation or abscess on echocardiogram or recent valvular regurgitation; and five minor criteria—(a) cardiac predisposition, such as previous valvular disease; (b) fever over  $38^{\circ}\text{C}$ ; (c) cutaneous vascular and/or immunological phenomena of endocarditis; (d) positive blood culture with pathogens not found with the major criteria (atypical organism); and (e) echocardiographic abnormalities other than those found with the major criteria. Positive diagnosis of endocarditis is based upon the presence of two major criteria, or one major criterion plus three minor criteria, or five minor criteria [10].

It might be useful to assess the extension of infectious disease (staging) in these patients by non-invasive whole body imaging, and  $^{18}\text{F}$ -FDG PET is a potential candidate for this purpose. To date, only three case reports have shown hot spots on leads related to confirmed infection [12–14]; no prospective series have been reported.

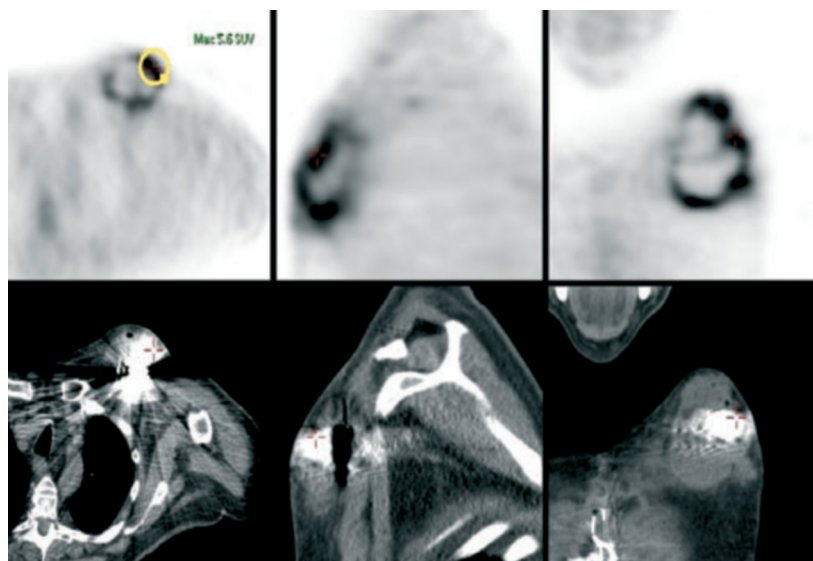
The aim of the present preliminary study was to evaluate the potential use of this imaging method by defining the best criteria for positive diagnosis. The results suggest that  $^{18}\text{F}$ -FDG PET shows high diagnostic accuracy when infection affects the box (Fig. 2) and is slightly less reliable when the leads are involved.

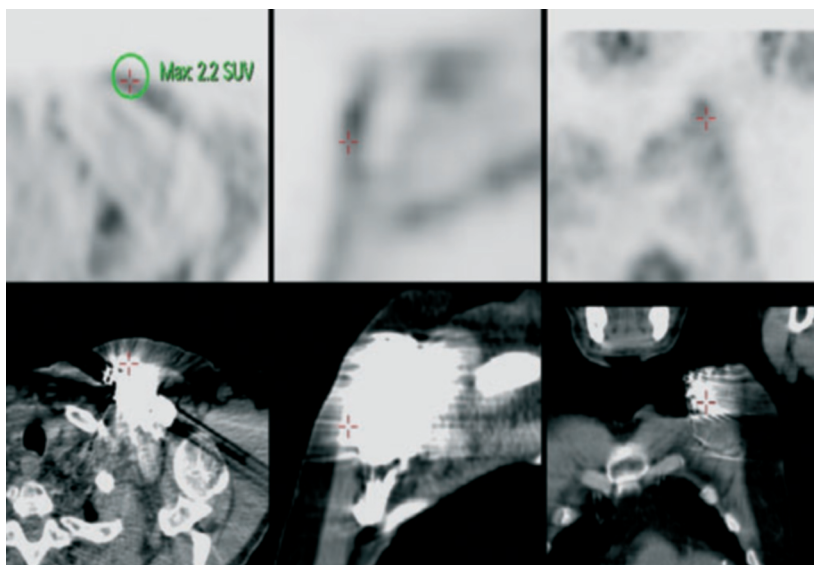
Physiologically (Fig. 3), slight  $^{18}\text{F}$ -FDG uptake may be observed around the box, particularly in front of the muscle interface in controls. False enhancement on attenuation-corrected images may be related to a metallic artefact resulting from the box itself, which can easily be prevented by comparison with non-attenuation-corrected images. Although uptake around the box is much higher in cases of infection

than in controls, the physiological uptake seen in controls might be confusing for inexperienced observers and could be explained by mild, non-specific inflammation caused by rubbing of skin and soft tissue against the box. Another possibility is diffusion of low-intensity impulses within adjacent muscular structures, leading to muscular activity of a low level but sufficient to generate a significant difference in muscular metabolism. Therefore,  $^{18}\text{F}$ -FDG uptake quantification might be useful during the learning-curve phase, as visual analysis requires a higher level of uptake than on other sites to allow a conclusion in favour of infection. In any case, because of the high uptake intensity in patients with infection and the size of the device itself, which is much larger than the resolution of the PET system, negative predictive value and reproducibility appear to be very high.

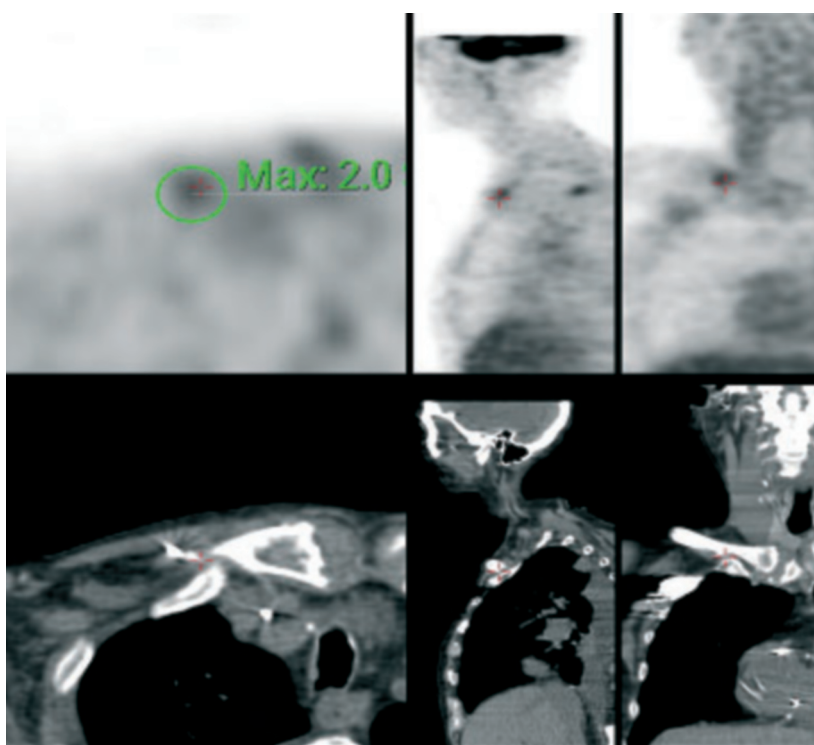
Diagnosis of lead infection represents a different challenge. First, the leads and the the vegetation are both very small, and may easily be below the theoretical resolution of the PET system. However, with PET imaging, current practice demonstrates that even an object that is small in comparison with the system's resolution may be seen if tracer uptake is very high. According to this hypothesis, the so-called partial volume effects, resulting from the mild spatial resolution of the PET system, may decrease the apparent uptake, explaining why the tracer uptake intensity on images in the present series was very mild, impairing interobserver reproducibility during the learning phase. Because of the individual variability in tracer uptake and in circulating tracer, as shown by the similar standard deviations of  $\text{SUV}_{\text{max}}$  in infected patients and in controls, quantification is not useful for positive diagnosis of lead infection, which is, rather, based visually, case by case, on the presence of low to moderate hot spots on the

**FIG. 2.** Box infection. Top: transverse (left), sagittal (medium) and coronal (right) positron emission tomography slices through the box. High [ $^{18}\text{F}$ ]fluorodeoxyglucose uptake indicates pocket infection. Bottom: corresponding computed tomography slices.





**FIG. 3.** Physiological uptake around the box (control patient). Top: transverse (left), sagittal (medium) and coronal (right) positron emission tomography slices through the box. The mild [ $^{18}\text{F}$ ]fluorodeoxyglucose uptake is usual and does not indicate any infectious process. Bottom: corresponding computed tomography slices. SUV, standard uptake value.



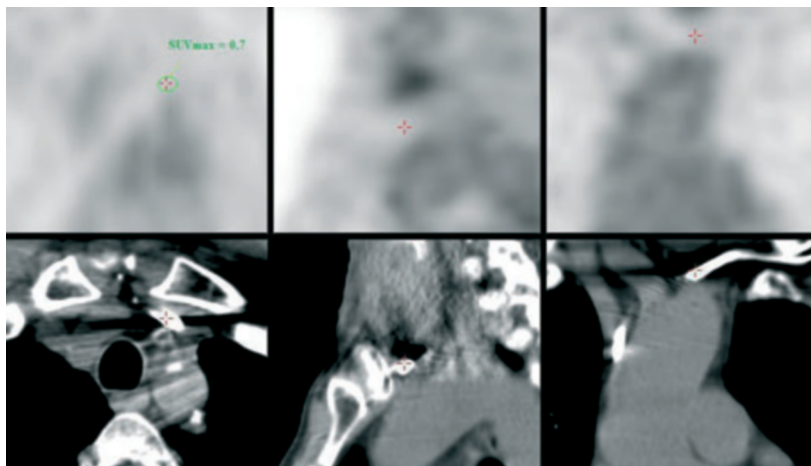
**FIG. 4.** Lead infection. Top: transverse (left), sagittal (medium) and coronal (right) slices displaying a focal hot spot on a lead (circle), indicating lead infection. Bottom: corresponding computed tomography slices.

lead itself (Figs 4 and 5). Because reproducibility for leads was weaker than for boxes, a learning curve is required, and dual interpretation should be performed.

Any intricate factor that can decrease tracer uptake entails a risk of false-negative cases. It should be emphasized that, in the present series, the false negatives were patients who received antibiotic therapy for the longest time. Although this needs to be confirmed in larger series,

interpretation of negative predictive values should be performed with care in cases of treatment duration of more than 7 days. One of the false-negative cases fulfilled only three of five Duke's criteria, but was finally considered to be positive by clinicians and treated accordingly. This classification as positive may be questionable, and had the effect of increasing the number of false negatives and thus decreasing the assessed accuracy of PET.

**FIG. 5.** Physiological lead aspect. Top: transverse (left), sagittal (medium) and coronal (right) slices displaying a non-infected lead (circle). Bottom: corresponding computed tomography slices.



Conversely, no false-positive cases were reported. Recent blood thrombi have been reported to show  $^{18}\text{F}$ -FDG uptake [15,16], but the inflammatory process that can be subsequently induced is probably less than that induced by septic foci. This point needs to be confirmed in further studies, as no such case actually occurred in the present series.

The study was not designed to address the impact of PET results on patient management: decisions were taken by clinicians independently of these results. A prospective study will be required to answer this question. Nevertheless, it was noteworthy that the only patient who was explanted and did not show device infection had negative PET findings, whereas the only one who was not initially explanted and did show device infection during follow-up had positive PET findings. As PET also revealed other infectious foci in three patients and an associated inflammatory disease in one, the change in patient management induced by PET could have concerned six of 21 patients (28%).

## Conclusion

$^{18}\text{F}$ -FDG PET imaging may be useful for the diagnosis of device infection after PM or ICD implantation. For boxes, sensitivity and specificity are optimal even though mild physiological uptake may be seen in normal cases. For leads, sensitivity and reproducibility are more problematic, and diagnosis is based upon visualization of mild focal uptake along the leads. Interpretation of negative cases should be cautious if patients have received prolonged antibiotherapy. Although the study was not designed for this purpose, management could have been modified by PET results in six of 21 patients.

## Transparency Declaration

Absence of conflicting interests for all coauthors.

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